

C6
E1
cont

~~N-((5S)-3-[3-fluoro-4-(1-[[(ethoxycarbonyl)methyl]imino]-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;~~
~~N-((5S)-3-[3-fluoro-4-(1-{{[(4-nitrophenyl)amino]carbonyl}imino}-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer ;~~
~~N-((5S)-3-[3-fluoro-4-N-[(aminocarbonyl)imino]-1-oxidohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;~~
~~N-((5S)-3-[3-fluoro-4-[1-[(aminocarbonyl)methyl]imino]-1-oxidohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;~~
~~N-((5S)-3-[3-fluoro-4-[1-[(2-hydroxyethyl)imino]-1-oxidohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;~~
~~N-((5S)-3-[3-fluoro-4-[1-(methylimino)-1-oxidohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)cyclopropanecarbothioamide, Z-isomer;~~
~~N-[((5S)-3-{3-fluoro-4-[1-[(methoxycarbonyl)imino]-1-oxidohexahydro-1λ⁴-thiopyran-4-yl]phenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]cyclopropanecarbothioamide, Z-isomer;~~
~~N-[((5S)-3-{3-fluoro-4-[1-[(phenylmethoxy)carbonyl]imino]-1-oxidohexahydro-1λ⁴-thiopyran-4-yl]phenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide, Z-isomer; or~~
~~N-((5S)-3-[3-fluoro-4-(1-{{[(benzylamino)carbonyl]imino}-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)acetamide, Z-isomer.~~

REMARKS

Claims 1-14, 16, 17, 22-25, 30-36, and 38-66 are currently pending. Reconsideration of the pending application is respectfully requested in view of the following remarks.

Applicants have amended claims 1, 9, 16, 47, 54, and 65 to address the Examiner's rejections, e.g., 1 q), 3 a), b), c), d), e), f), h) and i), made under 35 U.S.C. § 112, second paragraph. See the office action at pages 3-5. The remaining rejections will be addressed below.

Applicants note that the substituent Z in claim 47 is defined as S(=O)(=N-R₅) such that the valence of the nitrogen atom is correctly fulfilled. The structure for B in claim 47 merely illustrates the claimed stereochemistry for the (=O) and (=N-R₅) groups on the sulfur atom.

The reference to "formula I" in claim 66 includes correct antecedent basis since the claim references "a compound of formula I as shown in claim 47." Indeed, claim 30 and numerous issued U.S. Patents include similar claim language. See, for example, U.S. Patent No. 5,968,962.

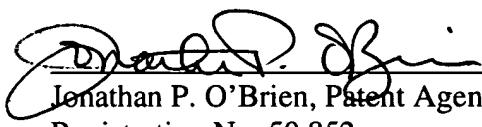
Claims 1-14, 16, 17, 22, 30-36, 38, 42, 47-56, 61, and 65 stand rejected under 35 U.S.C. § 112, first paragraph as "including subject matter which was not described in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention." In making this rejection, the Examiner contends that the phenyl substituents CF_3 and CH_3 are new matter with respect to the genus of independent claims 1 and 47. See the office action at page 4. Applicants respectfully disagree. At the time of filing, the Application contained a specific disclosure of CH_3 and CF_3 as possible substituents for phenyl groups. See the Specification at page 6, lines 8 and 9. Based upon this disclosure and the definition of formula I at page 3, lines 27-30, which lists other possible phenyl substituents, one skilled in the art would have reasoned that the generic description of the compounds of formula I included both those phenyl substituents at page 3 as well as those at page 10.

Withdrawal of this rejection is respectfully request in view of the foregoing remarks.

CONCLUSION

Claims 1-14, 16, 17, 22-25, 30-36, and 38-66 are now in condition for allowance, which action is respectfully request. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,



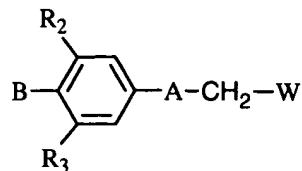
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Version with markings to show changes made

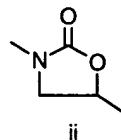
1. (TWICE AMENDED) A compound of formula I



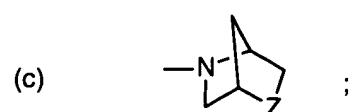
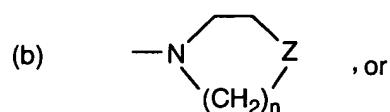
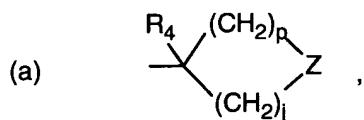
I

or a pharmaceutically acceptable salt thereof wherein:

A is a structure [i,] ii[, iii, or iv]



B is



W is NHC(=X)R₁, or -Y-het; X is O, or S; provided that when X is O, B is not the subsection

(b);

Y is NH, O, or S;

Z is S(=O)(=N-R₅);

R₁ is

- (a) H,
- (b) NH₂,
- (c) NHC₁₋₄alkyl,
- (d) C₁₋₄alkyl,
- (e) C₂₋₄alkenyl,
- (f) OC₁₋₄alkyl,
- (g) SC₁₋₄alkyl, or
- (h) (CH₂)_pC₃₋₆cycloalkyl;

at each occurrence, alkyl or cycloalkyl in R₁ is optionally substituted with one or more F, Cl or CN;

R₂ and R₃ are independently H, F, Cl, methyl or ethyl;

R₄ is H, CH₃, or F;

R₅ is

- (c) C(=O)C₁₋₄alkyl,
- (d) C(=O)OC₁₋₄alkyl,
- (e) C(=O)NHR₆, or
- (f) C(=S)NHR₆;

R₆ is H, C₁₋₄alkyl, or phenyl;

at each occurrence, alkyl in R₅ and R₆ is optionally substituted with one or more halo, CN, NO₂, phenyl, C₃₋₆ cycloalkyl, OR₇, C(=O)R₇, OC(=O)R₇, C(=O)OR₇, S(=O)_mR₇, S(=O)_mNR₇R₇, NR₇SO₂R₇, NR₇SO₂NR₇R₇, NR₇C(=O)R₇, C(=O)NR₇R₇, NR₇R₇, oxo, or oxime;

R₇ is H, C₁₋₄alkyl, or phenyl;

at each occurrence, phenyl is optionally substituted with one or more halo, CF₃, [CH3] CH₃, CN, NO₂, phenyl, C₃₋₆ cycloalkyl, OR₇, C(=O)R₇, OC(=O)R₇, C(=O)OR₇, S(=O)_mR₇, S(=O)_mNR₇R₇, NR₇SO₂R₇, NR₇SO₂NR₇R₇, NR₇C(=O)R₇, C(=O)NR₇R₇, or NR₇R₇;

het is a C-linked five- (5) membered heteroaryl ring having 1-4 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen, or het is a C-linked six (6) membered heteroaryl ring having 1-3 nitrogen atoms;

p is 0, 1, or 2;

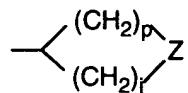
j is 1, 2, 3, 4, or 5; provided that j and p taken together are 2, 3, 4 or 5;

m is 0, 1, or 2; and

n is 2 or 3[; and ----- in structure iii is either a double bond or a single bond].

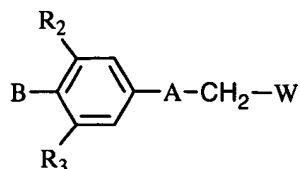
9. (ONCE AMENDED) A compound of claim 2-7 wherein X is an oxygen atom.

16. (ONCE AMENDED) A compound of claim 8 wherein structure B is



wherein Z is $\text{S}(=\text{O})(=\text{N}\text{R}_5)$.

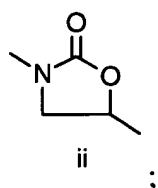
47. (ONCE AMENDED) [1.] A compound of formula II



II

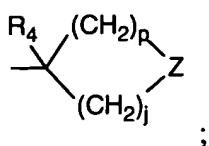
or a pharmaceutically acceptable salt thereof wherein:

A is a structure ii



;

B is



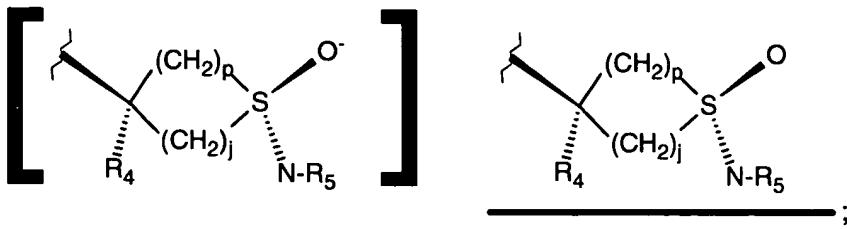
;

W is NHC(=X)R₁, or -Y-het;

X is O, or S;

Y is NH, O, or S;

Z is S(=O)(=N-R₅) and the B ring has the following stereochemistry



R₁ is

- (a) H,
- (b) NH₂,
- (c) NHC₁₋₄alkyl,
- (d) C₁₋₄alkyl,
- (e) C₂₋₄alkenyl,
- (f) OC₁₋₄alkyl,
- (g) SC₁₋₄alkyl, or
- (h) (CH₂)_pC₃₋₆cycloalkyl;

at each occurrence, alkyl or cycloalkyl in R₁ is optionally substituted with one or more F, Cl or CN;

R₂ and R₃ are independently H, F, Cl, methyl or ethyl;

R₄ is H, CH₃, or F;

R₅ is

- (a) H,
- (b) C₁₋₄alkyl,
- (c) C(=O)C₁₋₄alkyl,
- (d) C(=O)OC₁₋₄alkyl,
- (e) C(=O)NHR₆, or
- (f) C(=S)NHR₆;

R₆ is H, C₁₋₄alkyl, or phenyl;

at each occurrence, alkyl in R₅ and R₆ is optionally substituted with one or more halo, CN, NO₂, phenyl, C₃₋₆ cycloalkyl, OR₇, C(=O)R₇, OC(=O)R₇, C(=O)OR₇, S(=O)_mR₇, S(=O)_mNR₇R₇, NR₇SO₂R₇, NR₇SO₂NR₇R₇, NR₇C(=O)R₇, C(=O)NR₇R₇, NR₇R₇, oxo, or oxime;

R₇ is H, C₁₋₄alkyl, or phenyl;

at each occurrence, phenyl is optionally substituted with one or more halo, CF₃ [CH3], CH₃, CN, NO₂, phenyl, C₃₋₆ cycloalkyl, OR₇, C(=O)R₇, OC(=O)R₇, C(=O)OR₇, S(=O)_mR₇, S(=O)_mNR₇R₇, NR₇SO₂R₇, NR₇SO₂NR₇R₇, NR₇C(=O)R₇, C(=O)NR₇R₇, or NR₇R₇;

het is a C-linked five- (5) membered heteroaryl ring having 1-4 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen, or het is a C-linked six (6) membered heteroaryl ring having 1-3 nitrogen atoms;

p is 0, 1, or 2;

j is 1, 2, 3, 4, or 5; provided that j and p taken together are 2, 3, 4 or 5;

m is 0, 1, or 2[; and ---- in structure iii is either a double bond or a single bond.].

54. (ONCE AMENDED) The compound of claim 47 wherein X is an oxygen atom.

65. (TWICE AMENDED) A compound of claim 47 which is

N-((5S)-3-[3-fluoro-4-(1-imino-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)acetamide (Z)-isomer;

N-((5S)-3-[3-fluoro-4-(1-imino-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)ethanethioamide (Z)-isomer;

N-((5S)-3-[3-fluoro-4-(1-imino-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)propanethioamide (Z)-isomer;

N-((5S)-3-[3-fluoro-4-(1-imino-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)cyclopropanethioamide (Z)-isomer;

N-((5S)-3-[3-fluoro-4-[1-(acetylimino)-1-oxidohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)acetamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-[1-(methylimino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-[1-(acetylimino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-[1-(ethylimino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-[1-[(phenylmethyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-[1-[(3-phenylpropyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-(1-{{(methylamino)carbonyl}imino}-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-(1-[(methoxycarbonyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-(1-[[ethoxycarbonyl)methyl]imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-(1-{{[(4-nitrophenyl)amino]carbonyl}imino}-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer ;

N-((5*S*)-3-[3-fluoro-4-[1-[(aminocarbonyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-[1-[(aminocarbonyl)methyl]imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-[1-[(2-hydroxyethyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-[1-(methylimino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)cyclopropanecarbothioamide, Z-isomer;

N-((5*S*)-3-[3-fluoro-4-[1-[(methoxycarbonyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)cyclopropanecarbothioamide, Z-isomer;

N-[((5*S*)-3-{3-fluoro-4-[1-[(phenylmethoxy)carbonyl]imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide, Z-isomer; or
N-((5*S*)-3-[3-[**Fluoro**] **fluoro**-4-(1-[(benzylamino)carbonyl]imino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide, Z-isomer.